



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Charles D. Jones

Serial No.: 331,042

Filed : December 16, 1981

For : ANTIESTROGENIC AND ANTI-ANDROGENIC BENZOTHIOPHENE

Docket No.: X-5526A

Group Art Unit: 121

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SUPPLEMENTARY DISCLOSURE STATEMENT

GROUP 120

Commissioner of Patents and Trademarks

Washington, D. C. 20231

Sir:

Applicant cites the following patent application, article and United States patents to the Examiner as documents which are material to the present invention.

United States Patent Application 246,334, filed 3 April 1981 by the present inventor and M. E. Goettel, teaches a process for preparing the dihydroxy compound of the present invention. The process of that application, filed on the same day with the parent of the present application, is not the only operable process but is a preferred process. The present application describes the process of the Jones-Goettel application as one way to obtain the compounds of the present invention, and numerous examples of syntheses according to Jones-Goettel are in the present specification.

Claeys et al., Chimie Therapeutique, 377-84 (1972), describes some acylated benzothiophenes which are, to a degree, material to the compounds of the present invention. Claeys' compounds, however, have no hydroxy groups, bear halogen atoms on the benzoyl ring, and have only alkyl groups at the 2-position of the benzothiophene nucleus. Some of their compounds, however, such as number 15 for example, have a piperidino group on the

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side chain. The alkoxy group of their side chain, however, is of various lengths, and the piperidino group is always associated with a propoxy side chain.

U.S. Patent 3,920,707, of Descamps et al., shows a group of acylated benzofurans, which compounds have alkyl or cyclohexyl groups at the 2-position of the furan ring. Their compounds do not have hydroxy groups. The alkoxy portion of their acyl side chain has from 3 to 6 methylene groups, and thus excludes the ethoxy side chain of the compounds of the present invention. The patent teaches its compounds to be useful for the reduction of blood pressure and the control of angina.

U.S. Patent 3,947,470, of Brenner et al., shows benzo-thiophenes and benzofurans having an aminoalkoxybenzoyl side chain. It must be noted, however, that the patent shows only alkyl- or dialkylamino groups at the terminus of the side chain, and thus it does not suggest the piperidino ring which is a vital feature of the present invention.

It should also be noted that the patent does not show compounds having free hydroxy groups on the benzofuran or benzo-thiophene nucleus, but only alkoxy groups, among other substituents even less suggestive of the present invention.

U.S. Patent 4,001,426, of Brenner and Brush, shows benzo-thiophenes and benzofurans of a different type. Its compounds have a benzoyl group which can carry various small substituents, and an aminoalkoxyphenyl side chain. Thus, the compounds of this patent lack the basic acyl side chain which is a mandatory feature of the present invention. Further, the compounds of this patent also cannot bear hydroxy groups but only alkoxies or less pertinent small substituents.

The above two patents disclose their compounds to be useful as vasodilators, hypotensive agents and agents for the treatment of angina, and do not mention any activities at all related to the hormonal systems of the body.

U.S. Patent 3,983,245, of Ladd and Ross, shows another group of acylated benzothiophenes and benzofurans which cannot bear hydroxy groups on the nucleus. The compounds have an acyl side chain which differs from other amine-containing side chains, in that the nitrogen atom is at the exterior side of a polymethyleneaza group. The side chain, thus, could contain a piperidino ring, as in Examples 5 and 7 of the patent, but the nitrogen atom of the piperidine ring, substituted with a small alkyl group, is exterior and the piperidine ring is joined to the rest of the side chain by its 4-position carbon. Thus, the patent discloses compounds quite different from those of the present invention.

Finally, Belgian Patent 819,675, of Hill and Leev, shows yet another group of acylated benzofurans. These compounds have no hydroxy groups on the benzofuran nucleus compound, but can and often do have a hydroxy group or an alkanoyloxy group on the side chain itself. The examples of the patent show a strong preference for propoxy side chains. Example 33 shows a compound having a piperidino ring, in company with an acetoxo group on the propoxy chain. This patent also refers only to vasodilator, anti-angina and hypotensive activity.


Applicant cites the above documents to the Examiner in the hope that they will be useful in the substantive examination

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of this application, and also in planning the Examiner's search. The documents are believed to be material to the invention, to a degree, but to have no effect on its patentability.

Respectfully submitted,

  
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